The Listing of Claims

This listing of claims will replace all prior versions and listings of claims in the application.

Claims 1-103 (cancelled)

Claim 104 (previously presented) A method for inhibiting beta-secretase activity, comprising exposing said beta-secretase to an effective inhibitory amount of a compound according to claim 176.

Claim 105 (original) The method of claim 104, wherein said beta-secretase is exposed to said compound *in vitro*.

Claim 106 (original) The method of claim 104, wherein said beta-secretase is exposed to said compound in a cell.

Claim 107 (original) The method of claim 106, wherein said cell is in an animal.

Claim 108 (original) The method of claim 107, wherein said animal is a human.

Claims 109 (cancelled)

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Claim 110 (previously presented) A method for inhibiting cleavage of amyloid precursor protein (APP), in a reaction mixture, at a site between Met596 and Asp597, numbered for the APP-695 amino acid isotype; or at a corresponding site of an isotype or mutant thereof, comprising exposing said reaction mixture to an effective inhibitory amount of a compound according to claim 176.

Claim 111 (original) The method of claim 110, wherein said cleavage site is between Met652 and Asp653, numbered for the APP-751 isotype; between Met 671 and Asp 672, numbered for the APP-770 isotype; between Leu596 and Asp597 of the APP-695 Swedish Mutation; between Leu652 and Asp653 of the APP-751 Swedish Mutation; or between Leu671 and Asp672 of the APP-770 Swedish Mutation.

Claim 112 (original) The method of claim 110, wherein said reaction mixture is exposed *in vitro*.

Claim 113 (original) The method of claim 110, wherein said reaction mixture is exposed in a cell.

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Claim 114 (original) The method of claim 113, wherein said cell is an animal cell.

Claim 115 (original) The method of claim 114, wherein said cell is a human cell.

Claim 116 (previously presented) A method for inhibiting cleavage of amyloid precursor protein (APP), in a reaction mixture, at a site between Met596 and Asp597, numbered for the APP-695 amino acid isotype; or at a corresponding site of an isotype or mutant thereof, comprising exposing said reaction mixture to an effective inhibitory amount of a compound according to claim 176.

Claim 117 (original) The method of claim 116, wherein said cleavage site is between Met652 and Asp653, numbered for the APP-751 isotype; between Met 671 and Asp 672, numbered for the APP-770 isotype; between Leu596 and Asp597 of the APP-695 Swedish Mutation; between Leu652 and Asp653 of the APP-751 Swedish Mutation; or between Leu671 and Asp672 of the APP-770 Swedish Mutation.

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Claim 118 (original) The method of claim 116, wherein said reaction mixture is exposed *in vitro*.

Claim 119 (original) The method of claim 116, wherein said reaction mixture is exposed in a cell.

Claim 120 (original) The method of claim 118, wherein said cell is an animal cell.

Claim 121 (original) The method of claim 120, wherein said cell is a human cell.

Claim 122 (previously presented). A method for inhibiting production of amyloid beta peptide (A beta) in a cell, comprising administering to said cell an effective inhibitory amount of a compound according to claim 176.

Claim 123 (original) The method of claim 122, wherein said administering is to an animal.

Claim 124 (original) The method of claim 123, wherein said administering is to a human.

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Claims 125-129 (cancelled)

Claim 130 (previously presented) A method for inhibiting the production of beta-amyloid plaque in an animal, comprising administering to said animal an effective inhibitory amount of a compound according to claim 176.

Claim 131 (original) The method of claim 130, wherein said animal is a human.

Claims 132 (previously presented) A method for treating or preventing a disease characterized by beta-amyloid deposits in the brain comprising administering to a patient an effective therapeutic amount of a compound according to claim 176.

Claim 133 (previously presented) The method of claim 132, wherein said therapeutic amount is in the range of from about 0.1 to about 1500 mg/day.

Claim 134 (previously presented) The method of claim 132, wherein said therapeutic amount is in the range of from about 15 to about 1000 mg/day.

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Claim 135 (original) The method of claim 133, wherein said therapeutic amount is in the range of from about 1 to about 100 mg/day.

Claim 136 (original) The method of claim 135, wherein said therapeutic amount is in the range of from about 5 to about 50 mg/day.

Claim 137 (original) The method of claim 133, wherein said disease is Alzheimer's disease.

Claim 138 (original) The method of claim 132, wherein said disease is Mild Cognitive Impairment, Down's Syndrome, or Hereditary Cerebral Hemmorrhage with Amyloidosis of the Dutch Type.

Claims 139-145 (cancelled)

Claim 146 (previously presented) Beta-secretase complexed with a compound according to claim 176.

Claim 147 (cancelled)

Claim 148 (previously presented) A method for producing a beta-secretase complex comprising: exposing beta-secretase to a

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compound according to claim 176, or a pharmaceutically acceptable salt thereof in a reaction mixture under conditions suitable for the production of said complex.

Claim 149 (original) The method of claim 148, where said exposing is *in vitro*.

Claim 150 (original) The method of claim 149, wherein said reaction mixture is a cell.

Claims 151-157(cancelled)

Claim 158 (previously presented) A kit comprising a plurality of containers, each container comprising one or more unit dose of a compound according to claim 176.

Claim 159 (original) The kit of claim 158, wherein each container is adapted for oral delivery and comprises a tablet, gel, or capsule.

Claim 160 (previously presented) The kit of claim 158, wherein each container is adapted for parenteral delivery and comprises a depot product, syringe, ampoule, or vial.

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Claim 161 (original) The kit of claim 158, wherein each container is adapted for topical delivery and comprises a patch, medipad, ointment, or cream.

Claims 162-167 (cancelled)

Claim 168 (previously presented) A composition comprising a compound according to claim 176; and an inert diluent or edible carrier.

Claim 169 (original) The composition of claim 168, wherein said carrier is an oil.

Claim 170 (currently amended) A composition comprising a compound according to ~~claim 1~~ claim 176; and an inert diluent or edible carrier.

Claim 171 (original) The composition of claim 170, wherein said carrier is an oil.

Claims 172-175 (cancelled)

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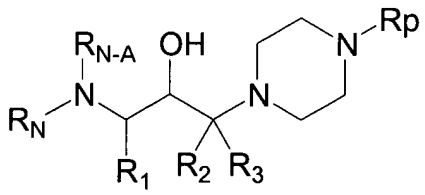
Claim 176 (previously presented) A compound of the formula



or a pharmaceutically acceptable salt thereof wherein

where R_p represents

(1) C_1-C_6 alkyl, C_2-C_6 alkenyl with one or two double bonds, or C_2-C_6 alkynyl with one or two triple bonds, each of which is optionally substituted with one, two, or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1\text{-}a}R_{1\text{-}b}$ where $R_{1\text{-}a}$ and $R_{1\text{-}b}$ are -H or C_1-C_6 alkyl,

(2) $-CO-(C_1\text{-}C_4$ alkyl),

(3) $-SO_2-NR_{p1}R_{p2}$ where R_{p1} and R_{p2} are hydrogen or C_1-C_6 alkyl, or

(4) $-CO-\ NR_{p1}R_{p2}$ where R_{p1} and R_{p2} are hydrogen or C_1-C_6;

R_1 is $-CH_2$-phenyl where the is phenyl optionally substituted with one, two, three, or four of

(A) C_1-C_6 alkyl optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, $-CF_3$,

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C_1-C_3 alkoxy, and-$NR_{1\text{-}a}R_{1\text{-}b}$ where $R_{1\text{-}a}$ and $R_{1\text{-}b}$ are independently -H or C_1-C_6 alkyl,

(B) C_2-C_6 alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, $-NR_{1\text{-}a}R_{1\text{-}b}$ where $R_{1\text{-}a}$ and $R_{1\text{-}b}$ are -H or C_1-C_6 alkyl,

(C) C_2-C_6 alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1\text{-}a}R_{1\text{-}b}$ where $R_{1\text{-}a}$ and $R_{1\text{-}b}$ are -H or C_1-C_6 alkyl,

(D) -F, Cl, -Br or -I,

(F) -C_1-C_6 alkoxy optionally substituted with one, two, or three -F,

(G) $-NR_{N\text{-}2}R_{N\text{-}3}$ where $R_{N\text{-}2}$ and $R_{N\text{-}3}$ are as defined below,

(H) -OH,

(I) -C≡N,

(J) C_3-C_7 cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1\text{-}a}R_{1\text{-}b}$ where $R_{1\text{-}a}$ and $R_{1\text{-}b}$ are -H or C_1-C_6 alkyl,

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(K) $-CO-(C_1-C_4$ alkyl),

(L) $-SO_2-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as defined above,

(M) $-CO-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as defined above, or

(N) $-SO_2-(C_1-C_4$ alkyl);

R_2 is

(I) -H,

(II) C_1-C_6 alkyl, optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, $-C\equiv N$, $-CF_3$, C_1-C_3 alkoxy, and-$NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as defined above,

(III) $-(CH_2)_{0-4}-R_{2-1}$ where R_{2-1} is R_{1-aryl} or $R_{1-heteroaryl}$, where R_{1-aryl} is is phenyl, 1-naphthyl, 2-naphthyl and indanyl, indenyl, dihydronaphthalyl, or tetralinyl optionally substituted with one, two, three, or four of the following substituents on the aryl ring:

(A) C_1-C_6 alkyl optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, $-C\equiv N$, $-CF_3$, C_1-C_3 alkoxy, and-$NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as defined above,

(B) C_2-C_6 alkenyl with one or two double bonds, optionally substituted with one, two or three

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substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, $-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are -H or C_1-C_6 alkyl,

(C) C_2-C_6 alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are -H or C_1-C_6 alkyl,

(D) -F, Cl, -Br or -I,

(F) -C_1-C_6 alkoxy optionally substituted with one, two, or three -F,

(G) $-NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are as defined below,

(H) -OH,

(I) -C≡N,

(J) C_3-C_7 cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are -H or C_1-C_6 alkyl,

(K) -CO-(C_1-C_4 alkyl),

(L) $-SO_2-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as defined above,

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(M) $-CO-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as defined above, or

(N) $-SO_2-(C_1-C_4$ alkyl); and

$R_{1\text{-heteroaryl}}$ is selected from the group consisting of pyridinyl, pyrimidinyl, quinolinyl, benzothienyl indolyl, indolinyl, pyridazinyl, pyrazinyl, isoquinolyl, quinazolinyl, quinoxalinyl, phthalazinyl, imidazolyl, isoxazolyl, pyrazolyl, oxazolyl, thiazolyl, indolizinyl, indazolyl, benzothiazolyl, benzimidazolyl, benzofuranyl, furanyl, thienyl, pyrrolyl, oxadiazolyl, thiadiazolyl, triazolyl, tetrazolyl, oxazolopyridinyl, imidazopyridinyl, isothiazolyl, naphthyridinyl, cinnolinyl, carbazolyl, beta-carbolinyl, isochromanyl, chromanyl, tetrahydroisoquinolinyl, isoindolinyl, isobenzotetrahydrofuranyl, isobenzotetrahydrothienyl, isobenzothienyl, benzoxazolyl, pyridopyridinyl, benzotetrahydrofuranyl, benzotetrahydrothienyl, purinyl, benzodioxolyl, triazinyl, phenoxazinyl, phenothiazinyl, pteridinyl, benzothiazolyl, imidazopyridinyl, imidazothiazolyl, dihydrobenzisoxazinyl, benzisoxazinyl, benzoxazinyl,

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dihydrobenzisothiazinyl, benzopyranyl, benzothiopyranyl, coumarinyl, isocoumarinyl, chromonyl, chromanonyl, pyridinyl-N-oxide, tetrahydroquinolinyl dihydroquinolinyl, dihydroquinolinonyl dihydroisoquinolinonyl dihydrocoumarinyl, dihydroisocoumarinyl isoindolinonyl benzodioxanyl, benzoxazolinonyl pyrrolyl N-oxide, pyrimidinyl N-oxide, pyridazinyl N-oxide, pyrazinyl N-oxide, quinolinyl N-oxide, indolyl N-oxide, indolinyl N-oxide, isoquinolyl N-oxide, quinazolinyl N-oxide, quinoxalinyl N-oxide, phthalazinyl N-oxide, imidazolyl N-oxide, isoxazolyl N-oxide, oxazolyl N-oxide, thiazolyl N-oxide, indolizinyl N-oxide, indazolyl N-oxide, benzothiazolyl N-oxide, benzimidazolyl N-oxide, pyrrolyl N-oxide, oxadiazolyl N-oxide, thiadiazolyl N-oxide, triazolyl N-oxide, tetrazolyl N-oxide, benzothiopyranyl S-oxide, and benzothiopyranyl S,S-dioxide, and

heteroaryl is optionally substituted with one, two, three, or four of

(1) C_1-C_6 alkyl optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH,

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-SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and-$NR_{1\text{-}a}R_{1\text{-}b}$ where $R_{1\text{-}a}$ and $R_{1\text{-}b}$ are as defined above,

(2) C_2-C_6 alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1\text{-}a}R_{1\text{-}b}$ where $R_{1\text{-}a}$ and $R_{1\text{-}b}$ are -H or C_1-C_6 alkyl,

(3) C_2-C_6 alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and-$NR_{1\text{-}a}R_{1\text{-}b}$ where $R_{1\text{-}a}$ and $R_{1\text{-}b}$ are -H or C_1-C_6 alkyl,

(4) -F, Cl, -BR, or -I,

(6) -C_1-C_6 alkoxy optionally substituted with one, two, or three -F,

(7) $-NR_{N\text{-}2}R_{N\text{-}3}$ where $R_{N\text{-}2}$ and $R_{N\text{-}3}$ are as defined below,

(8) -OH,

(9) -C≡N,

(10) C_3-C_7 cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1\text{-}a}R_{1\text{-}b}$ where $R_{1\text{-}a}$ and $R_{1\text{-}b}$ are -H or C_1-C_6 alkyl,

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(312) 913-0001

(11) $-CO-(C_1-C_4$ alkyl),

(12) $-SO_2-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as defined above,

(13) $-CO-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as defined above, or

(14) $-SO_2-(C_1-C_4$ alkyl), with the proviso that when n_1 is zero $R_{1\text{-heteroaryl}}$ is not bonded to the carbon chain by nitrogen;

(IV) C_2-C_6 alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are -H or C_1-C_6 alkyl,

(V) C_2-C_6 alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are -H or C_1-C_6 alkyl, or

(VI) $-(CH_2)_{0-4}-$ C_3-C_7 cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are -H or C_1-C_6 alkyl,

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R_3 is

(I) -H,

(II) C_1-C_6 alkyl, optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1\text{-}a}R_{1\text{-}b}$ where $R_{1\text{-}a}$ and $R_{1\text{-}b}$ are as defined above,

(III) $-(CH_2)_{0\text{-}4}$-$R_{2\text{-}1}$ where $R_{2\text{-}1}$ is $R_{1\text{-aryl}}$ or $R_{1\text{-heteroaryl}}$ where $R_{1\text{-aryl}}$ and $R_{1\text{-heteroaryl}}$ are as defined above;

(IV) C_2-C_6 alkenyl with one or two double bonds,

(V) C_2-C_6 alkynyl with one or two triple bonds, or

(VI) $-(CH_2)_{0\text{-}4}$- C_3-C_7 cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1\text{-}a}R_{1\text{-}b}$ where $R_{1\text{-}a}$ and $R_{1\text{-}b}$ are -H or C_1-C_6 alkyl;

R_N is $R_{N\text{-}1}$-CO-;

where $R_{N\text{-}1}$ is selected from the group consisting of:

(A) $R_{N\text{-aryl}}$ where $R_{N\text{-aryl}}$ is phenyl, 1-naphthyl, 2-naphthyl, tetralinyl, indanyl, or 6,7,8,9-tetrahydro-5H-benzo[a]cycloheptenyl, or dihydronaphthyl optionally substituted with one, two or three of the following substituents which can be the same or different and are:

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(1) C_1-C_6 alkyl, optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF_3, C_1-C_3 alkoxy, and -$NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as defined above,

(2) -OH,

(3) -NO_2,

(4) -F, -Cl, -Br, or -I,

(5) -CO-OH,

(6) -C≡N,

(7) -$(CH_2)_{0-4}$-CO-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are the same or different and are selected from the group consisting of:

(a) -H,

(b) -C_1-C_6 alkyl optionally substituted with one substituent selected from the group consisting of:

(i) -OH, and

(ii) -NH_2,

(c) -C_1-C_6 alkyl optionally substituted with one to three of -F, -Cl, -Br, or -I,

(d) -C_3-C_7 cycloalkyl,

(e) -(C_1-C_2 alkyl)-(C_3-C_7 cycloalkyl),

(f) -(C_1-C_6 alkyl)-O-(C_1-C_3 alkyl),

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300 S. Wacker Drive
Chicago, IL 60606
(312) 913-0001

(g) $-C_2-C_6$ alkenyl with one or two double bonds,

(h) $-C_2-C_6$ alkynyl with one or two triple bonds,

(i) $-C_1-C_6$ alkyl chain with one double bond and one triple bond,

(j) $-R_{1\text{-aryl}}$ where $R_{1\text{-aryl}}$ is as defined above, and

(k) $-R_{1\text{-heteroaryl}}$ where $R_{1\text{-heteroaryl}}$ is as defined above,

(8) $-(CH_2)_{0-4}-CO-(C_1-C_{12}$ alkyl),

(9) $-(CH_2)_{0-4}-CO-(C_2-C_{12}$ alkenyl with one, two or three double bonds),

(10) $-(CH_2)_{0-4}-CO-(C_2-C_{12}$ alkynyl with one, two or three triple bonds),

(11) $-(CH_2)_{0-4}-CO-(C_3-C_7$ cycloalkyl),

(12) $-(CH_2)_{0-4}-CO-R_{1\text{-aryl}}$ where $R_{1\text{-aryl}}$ is as defined above,

(13) $-(CH_2)_{0-4}-CO-R_{1\text{-heteroaryl}}$ where $R_{1\text{-heteroaryl}}$ is as defined above,

(14) $-(CH_2)_{0-4}-CO-R_{1\text{-heterocycle}}$ where $R_{1\text{-heterocycle}}$ is as defined above,

(15) $-(CH_2)_{0-4}-CO-R_{N-4}$ where R_{N-4} is selected from the group consisting of morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl, homomorpholinyl, homothiomorpholinyl, homothiomorpholinyl S-oxide, homothiomorpholinyl S,S-dioxide, pyrrolinyl and pyrrolidinyl where each group is optionally

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300 S. Wacker Drive
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(312) 913-0001

substituted with one, two, three, or four of: C_1-C_6 alkyl,

(16) $-(CH_2)_{0-4}$-CO-O-R_{N-5} where R_{N-5} is selected from the group consisting of:

(a) C_1-C_6 alkyl,

(b) $-(CH_2)_{0-2}-(R_{1\text{-aryl}})$ where $R_{1\text{-aryl}}$ is as defined above,

(c) C_2-C_6 alkenyl containing one or two double bonds,

(d) C_2-C_6 alkynyl containing one or two triple bonds,

(e) C_3-C_7 cycloalkyl,

(f) $-(CH_2)_{0-2}-(R_{1\text{-heteroaryl}})$ where $R_{1\text{-heteroaryl}}$ is as defined above,

(17) $-(CH_2)_{0-4}$-SO_2-$NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} are as defined above,

(18) $-(CH_2)_{0-4}$-SO-(C_1-C_8 alkyl),

(19) $-(CH_2)_{0-4}$-SO_2-(C_1-C_{12} alkyl),

(20) $-(CH_2)_{0-4}$-SO_2-(C_3-C_7 cycloalkyl),

(21) $-(CH_2)_{0-4}$-N(H or R_{N-5})-CO-O-R_{N-5} where R_{N-5} can be the same or different and is as defined above,

(22) $-(CH_2)_{0-4}$-N(H or R_{N-5})-CO-N(R_{N-5})$_2$, where R_{N-5} can be the same or different and is as defined above,

(23) $-(CH_2)_{0-4}$-N-CS-N(R_{N-5})$_2$, where R_{N-5} can be the same or different and is as defined above,

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300 S. Wacker Drive
Chicago, IL 60606
(312) 913-0001

(24) $-(CH_2)_{0-4}-N(-H \text{ or } R_{N-5})-CO-R_{N-2}$ where R_{N-5} and R_{N-2} can be the same or different and are as defined above,

(25) $-(CH_2)_{0-4}-NR_{N-2}R_{N-3}$ where R_{N-2} and R_{N-3} can be the same or different and are as defined above,

(26) $-(CH_2)_{0-4}-R_{N-4}$ where R_{N-4} is as defined above,

(27) $-(CH_2)_{0-4}-O-CO-(C_1-C_6 \text{ alkyl})$,

(28) $-(CH_2)_{0-4}-O-P(O)-(OR_{N\text{-}aryl\text{-}1})_2$ where $R_{N\text{-}aryl\text{-}1}$ is -H or C_1-C_4 alkyl,

(29) $-(CH_2)_{0-4}-O-CO-N(R_{N-5})_2$ where R_{N-5} is as defined above,

(30) $-(CH_2)_{0-4}-O-CS-N(R_{N-5})_2$ where R_{N-5} is as defined above,

(31) $-(CH_2)_{0-4}-O-(R_{N-5})_2$ where R_{N-5} is as defined above,

(32) $-(CH_2)_{0-4}-O-(R_{N-5})_2-COOH$ where R_{N-5} is as defined above,

(33) $-(CH_2)_{0-4}-S-(R_{N-5})_2$ where R_{N-5} is as defined above,

(34) $-(CH_2)_{0-4}-O-(C_1-C_6$ alkyl optionally substituted with one, two, three, four, or five -F),

(35) C_3-C_7 cycloalkyl,

(36) C_2-C_6 alkenyl with one or two double bonds optionally substituted with C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, or $-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as defined above,

(37) C_2-C_6 alkynyl with one or two triple bonds optionally substituted with C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH,

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300 S. Wacker Drive
Chicago, IL 60606
(312) 913-0001

-SH, -C≡N, -CF_3, C_1-C_3 alkoxy, or -$NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as defined above,

(38) -$(CH_2)_{0-4}$-N(-H or R_{N-5})-SO_2-R_{N-2} where R_{N-5} and R_{N-2} can be the same of different and are as described above, or

(39) -$(CH_2)_{0-4}$- C_3-C_7 cycloalkyl,

(B) -$R_{N\text{-}heteroaryl}$, where $R_{N\text{-}heteroaryl}$ is selected from the group as defined above in $R_{1\text{-}heteroaryl}$ and where the $R_{N\text{-}heteroaryl}$ group is bonded by any atom of the parent $R_{N\text{-}heteroaryl}$ group substituted by hydrogen such that the new bond to the $R_{N\text{-}heteroaryl}$ group replaces the hydrogen atom and its bond, where heteroaryl is optionally substituted with one, two, three, or four of the groups (1)-(39) defined above as optional substituents on $R_{N\text{-}aryl}$;

(C) $R_{N\text{-}aryl}$-W-$R_{N\text{-}aryl}$,

(D) $R_{N\text{-}aryl}$-W-$R_{N\text{-}heteroaryl}$,

(E) $R_{N\text{-}aryl}$-W-$R_{N\text{-}1\text{-}heterocycle}$, where $R_{n\text{-}1\text{-}heterocycle}$ is the same as $R_{1\text{-}heterocycle}$, as defined above,

(F) $R_{N\text{-}heteroaryl}$-W-$R_{N\text{-}aryl}$,

(G) $R_{N\text{-}heteroaryl}$-W-$R_{N\text{-}heteroaryl}$,

(H) $R_{N\text{-}heteroaryl}$-W-$R_{1\text{-}heterocycle}$,

(I) $R_{1\text{-}heterocycle}$-W-$R_{N\text{-}aryl}$,

(J) $R_{1\text{-}heterocycle}$-W-$R_{N\text{-}heteroaryl}$, and

(K) $R_{1\text{-}heterocycle}$-W-$R_{1\text{-}heterocycle}$,

McDonnell Boehnen Hulbert & Berghoff
300 S. Wacker Drive
Chicago, IL 60606
(312) 913-0001

where W is

$-(CH_2)_{0-4}-$,

$-O-$,

$-S(O)_{0-2}-$,

$-N(R_{N-5})-$ where R_{N-5} is as defined above, or

$-CO-$;

R_{N-A} is selected from the group consisting of H, C_1 - C_{10} alkyl, C_2-C_{10} alkenyl and alkynyl, phenyl, C_1 - C_4 alkyl-R_{N-aryl}, C_1-C_4 alkyl-$R_{N-heteroaryl}$, C_1 - C_4 alkyl-C_3-C_7 cycloalkyl and C_1-C_4 alkyl-$R_{1-heterocycle}$, wherein each multi-atom group may be optionally substituted with one, two, or three substituents independently selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, $-C(O)O-R_{1-a}$, and $-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are -H, C_1-C_6 alkyl or phenyl.

Claim 177 (previously presented) A compound of claim 176, wherein R_1 is substituted with two -F.

Claim 178. (previously presented) A compound of claim 177, wherein the -F substitutions are on the -3 and -5 positions.

McDonnell Boehnen Hulbert & Berghoff
300 S. Wacker Drive
Chicago, IL 60606
(312) 913-0001

Claim 179 (previously presented) A compound of claim 176, wherein R_2 and R_3 are both -H.

Claim 180 (previously presented) A compound according to claim 176, wherein R_p is C_1-C_8 alkyl.

Claim 181 (previously presented) A compound of claim 176, where R_{N-1} is phenyl and the phenyl is attached to the carbonyl at the 1-position and substituted with one -CO-$NR_{N-2}R_{N-3}$ group.

Claim 182 (previously presented) A compound according to claim 176, where R_{N-1} is phenyl and the phenyl is (a) attached to the carbonyl at the 1-position, (b) substituted with one -CO-$NR_{N-2}R_{N-3}$ group in the 3-position, and (c) substituted with methyl at the 5-position.

Claim 183 (previously presented) A compound according to claim 181, wherein R_{N-2} and R_{N-3} are the same and are C_3 alkyl.

Claim 184 (previously presented) A compound according to claim 183, wherein R_{N-2} and R_{N-3} are the same and are C_3 alkyl.

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300 S. Wacker Drive
Chicago, IL 60606
(312) 913-0001

Claim 185 (previously presented) A compound according to claim 176, which is

N^1-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-(4-methyl-1-piperazinyl)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide;

N^1-{(1S,2R)-1-benzyl-3-[4-(4-fluorophenyl)-1-piperazinyl]-2-hydroxypropyl}-N^3,N^3-dipropylisophthalamide; or

a pharmaceutically acceptable salt thereof.

Claim 186 (previously presented) A method for treating a patient who has Alzheimer's disease, delaying development of Alzheimer's disease in a patient of predisposed to development of the disease, preventing a patient from developing Alzheimer's disease, treating a patient with mild cognitive impairment (MCI), preventing or delaying the onset of Alzheimer's disease in those who would progress from MCI to AD, treating Down's syndrome, treating humans who have Hereditary Cerebral Hemorrhage with Amyloidosis of the Dutch-Type, treating cerebral amyloid angiopathy and preventing its potential consequences, i.e. single and recurrent lobar hemorrhages, treating other degenerative dementias, including dementias of mixed vascular and degenerative origin, dementia associated with Parkinson's disease, dementia associated with progressive supranuclear palsy, dementia associated with cortical basal degeneration,

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Chicago, IL 60606
(312) 913-0001

diffuse Lewy body type of Alzheimer's disease and who is in need of such treatment, the method comprising administration of a therapeutically effective amount of a compound according to claim 176.

Claim 187 (previously presented) A method of treatment according to claim 186, wherein the disease is Alzheimer's disease.

Claim 188 (previously presented) A method of treatment according to claim 186, wherein the method is preventing a disease from developing.

Claim 189 (previously presented) A method of treatment according to claim 186, wherein the therapeutically effective amount for oral administration is from about 0.1 mg/day to about 1,000 mg/day; for parenteral, sublingual, intranasal, intrathecal administration is from about 0.5 to about 100 mg/day; for depo administration and implants is from about 0.5 mg/day to about 50 mg/day; for topical administration is from about 0.5 mg/day to about 200 mg/day; for rectal administration is from about 0.5 mg to about 500 mg.

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(312) 913-0001

Claim 190 (previously presented) A method of treatment according to claim 189, wherein the therapeutically effective amount for oral administration is from about 1 mg/day to about 100 mg/day and for parenteral administration is from about 5 to about 50 mg daily.

Claim 191 (previously presented) A method of treatment according to claim 189 where the therapeutically effective amount for oral administration is from about 5 mg/day to about 50 mg/day.

Claim 192 (previously presented) A method according to claim 186, wherein R_1 is substituted with two -F.

Claim 193. (previously presented) A method according to claim 186, wherein the -F substitutions are on the -3 and -5 positions.

Claim 194 (previously presented) A method according to claim 186, wherein R_2 and R_3 are both -H.

Claim 195 (previously presented) A method according to claim 186, wherein R_p is C_1-C_8 alkyl.

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Chicago, IL 60606
(312) 913-0001

Claim 196 (previously presented) A method according to claim 186, where R_{N-1} is phenyl and the phenyl is attached to the carbonyl at the 1-position and substituted with one -CO-$NR_{N-2}R_{N-3}$ group.

Claim 197 (previously presented) A method according to claim 186, where R_{N-1} is phenyl and the phenyl is (a) attached to the carbonyl at the 1-position, (b) substituted with one -CO-$NR_{N-2}R_{N-3}$ group in the 3-position, and (c) substituted with methyl at the 5-position.

Claim 198 (previously presented) A method according to claim 197, wherein R_{N-2} and R_{N-3} are the same and are C_3 alkyl.

Claim 199 (previously presented) A compound according to claim 198, wherein R_{N-2} and R_{N-3} are the same and are C_3 alkyl.

Claim 200. (previously presented) A method according to claim 186 where the pharmaceutically acceptable salt is selected from the group consisting of salts of the following acids: acetic, aspartic, benzenesulfonic, benzoic, bicarbonic, bisulfuric, bitartaric, butyric, calcium edetate, camsylic,

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(312) 913-0001

carbonic, chlorobenzoic, citric, edetic, edisylic, estolic, esyl, esylic, formic, fumaric, gluceptic, gluconic, glutamic, glycollylarsanilic, hexamic, hexylresorcinoic, hydrabamic, hydrobromic, hydrochloric, hydroiodic, hydroxynaphthoic, isethionic, lactic, lactobionic, maleic, malic, malonic, mandelic, methanesulfonic, methylnitric, methylsulfuric, mucic, muconic, napsylic, nitric, oxalic, p-nitromethanesulfonic, pamoic, pantothenic, phosphoric, monohydrogen phosphoric, dihydrogen phosphoric, phthalic, polygalactouronic, propionic, salicylic, stearic, succinic, sulfamic, sulfanilic, sulfonic, sulfuric, tannic, tartaric, teoclic and toluenesulfonic.

Claim 201 (previously presented) A method according to claim 186, where the compound is

N^1-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-(4-methyl-1-piperazinyl)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide;

N^1-{(1S,2R)-1-benzyl-3-[4-(4-fluorophenyl)-1-piperazinyl]-2-hydroxypropyl}-N^3,N^3-dipropylisophthalamide; or

a pharmaceutically acceptable salt thereof.

Claim 202 (previously presented) A method for inhibiting beta-secretase activity, comprising exposing said beta-secretase

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(312) 913-0001

to an effective inhibitory amount of a compound according to claim 176.

Claim 203 (previously presented) The method of claim 202, wherein said beta-secretase is exposed to said compound *in vitro*.

Claim 204 (previously presented) The method of claim 202, wherein said beta-secretase is exposed to said compound in a cell.

Claim 205 (previously presented) The method of claim 204, wherein said cell is in an animal.

Claim 206 (previously presented) The method of claim 205, wherein said animal is a human.

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